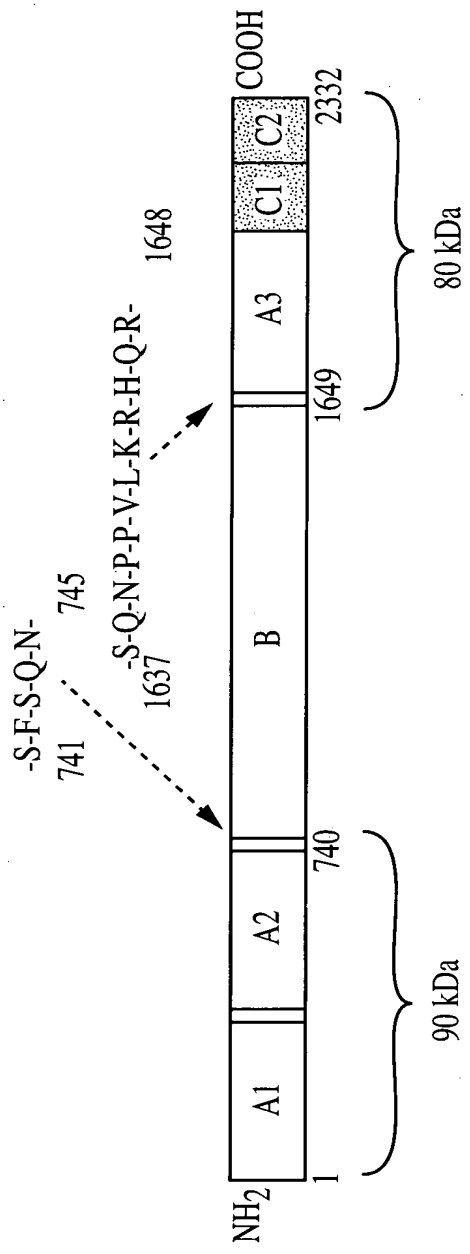
NH2
A1
A2
B
A3
C1
C2
COOH
1
740
741
745
1637
1648
1649
2332
90 kDa
80 kDa
-S-F-S-Q-N-
-S-Q-N-P-P-V-L-K-R-H-Q-R-

FIG. 1

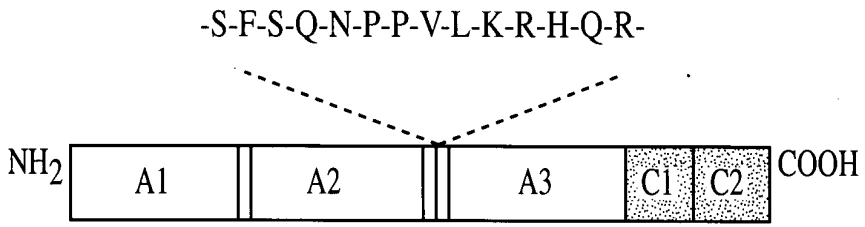

FIG. 2

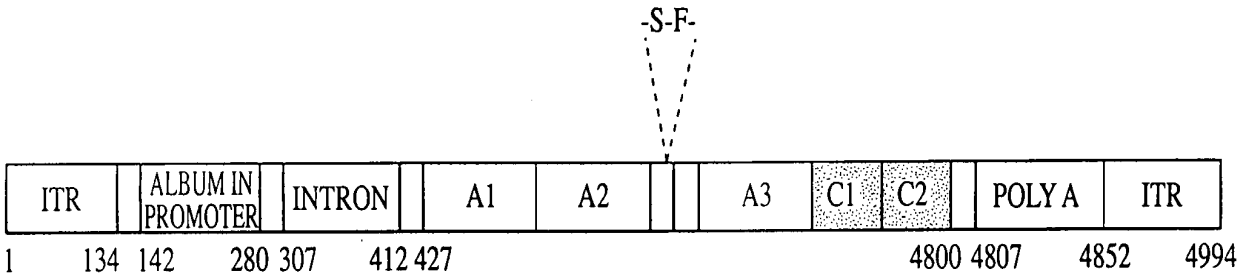
-S-F-
ITR
ALBUM IN PROMOTER
INTRON
A1
A2
A3
C1
C2
POLY A
ITR
1
134
142
280
307
412
427
4800
4807
4852
4994

FIG. 3

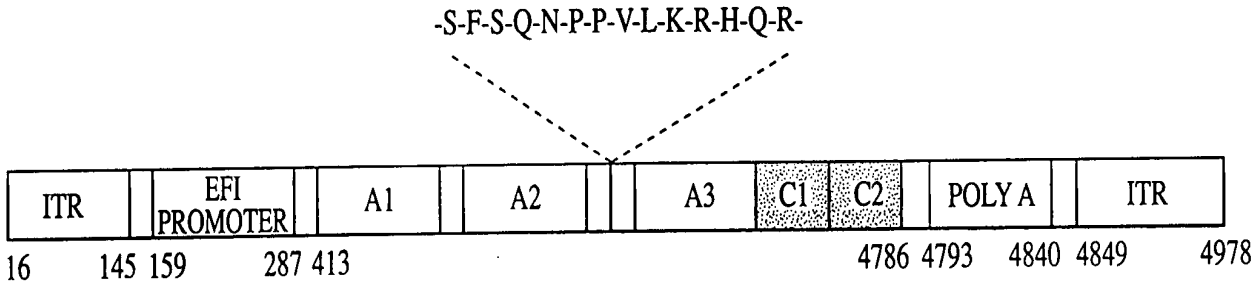
-S-F-S-Q-N-P-P-V-L-K-R-H-Q-R-
ITR
EFI PROMOTER
A1
A2
A3
C1
C2
POLY A
ITR
16
145
159
287
413
4786
4793
4840
4849
4978

FIG. 4

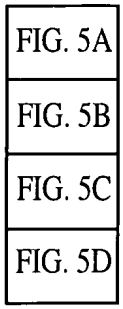

FIG. 5

CAGCTGCGCGCTCGCTCGCTCACTGAGGCCGCCCGGGCAAAGCCCGGGCGTCGGGCGACCTTTGGTCGCCCGGCCTCAGT
GAGCGAGCGAGCGCGCAGAGAGGGAGTGGCCAACTCCATCACTAGGGGTTCCTGCGGCCGCCCAGGGAATGTTTGTTCTT
AAATACCATCCAGGGAATGTTTGTTCTTAAATACCATCCAGGGAATGTTTGTTCTTAAATACCATCTACAGTTATTGGTT
AAAGAAGTATATTAGAGCGAGTCTTTCTGCACACAGATCACCTTTCCGGGTGCCGCCCCTAGGCAGGTAAGTGCCGTGTG
TGGTTCCCGCGGGCCTGGCCTCTTTACGGGTTATGGCCCTTGCGTGCCTTGAATTACTGACACTGACATCCACTTTTTCT
TTTTCTCCACAGGTATCGATTCCACCATGCAAATAGAGCTCTCCACCTGCTTCTTTCTGTGCCTTTTGCGATTCTGCTTT
AGTGCCACCAGAAGATACTACCTGGGTGCAGTGGAACTGTCATGGGACTATATGCAAAGTGATCTCGGTGAGCTGCCTGT
GGACGCAAGATTTCCTCCTAGAGTGCCAAAATCTTTTCCATTCAACACCTCAGTCGTGTACAAAAAGACTCTGTTTGTAG
AATTCACGGATCACCTTTTCAACATCGCTAAGCCAAGGCCACCCTGGATGGGTCTGCTAGGTCCTACCATCCAGGCTGAG
GTTTATGATACAGTGGTCATTACACTTAAGAACATGGCTTCCCATCCTGTCAGTCTTCATGCTGTTGGTGTATCCTACTG
GAAAGCTTCTGAGGGAGCTGAATATGATGATCAGACCAGTCAAAGGGAGAAAGAAGATGATAAAGTCTTCCCTGGTGGAA
GCCATACATATGTCTGGCAGGTCCTGAAAGAGAATGGTCCAATGGCCTCTGACCCACTGTGCCTTACCTACTCATATCTT
TCTCATGTGGACCTGGTAAAAGACTTGAATTCAGGCCTCATTGGAGCCCTACTAGTATGTAGAGAAGGGAGTCTGGCCAA
GGAAAAGACACAGACCTTGCACAAATTTATACTACTTTTTGCTGTATTTGATGAAGGGAAAAGTTGGCACTCAGAAACAA
AGAACTCCTTGATGCAGGATAGGGATGCTGCATCTGCTCGGGCCTGGCCTAAAATGCACACAGTCAATGGTTATGTAAAC
AGGTCTCTGCCAGGTCTGATTGGATGCCACAGGAAATCAGTCTATTGGCATGTGATTGGAATGGGCACCACTCCTGAAGT
GCACTCAATATTCCTCGAAGGTCACACATTTCTTGTGAGGAACCATCGCCAGGCGTCCTTGGAAATCTCGCCAATAACTT
TCCTTACTGCTCAAACACTCTTGATGGACCTTGGACAGTTTCTACTGTTTTGTCATATCTCTTCCCACCAACATGATGGC
ATGGAAGCTTATGTCAAAGTAGACAGCTGTCCAGAGGAACCCCAACTACGAATGAAAAATAATGAAGAAGCGGAAGACTA
TGATGATGATCTTACTGATTCTGAAATGGATGTGGTCAGGTTTGATGATGACAACTCTCCTTCCTTTATCCAAATTCGCT
CAGTTGCCAAGAAGCATCCTAAAACTTGGGTACATTACATTGCTGCTGAAGAGGAGGACTGGGACTATGCTCCCTTAGTC
CTCGCCCCCGATGACAGAAGTTATAAAAGTCAATATTTGAACAATGGCCCTCAGCGGATTGGTAGGAAGTACAAAAAAGT
CCGATTTATGGCATACACAGATGAAACCTTTAAGACTCGTGAAGCTATTCAGCATGAATCAGGAATCTTGGGACCTTTAC
TTTATGGGGAAGTTGGAGACACACTGTTGATTATATTTAAGAATCAAGCAAGCAGACCATATAACATCTACCCTCACGGA
ATCACTGATGTCCGTCCTTTGTATTCAAGGAGATTACCAAAAGGTGTAAAACATTTGAAGGATTTTCCAATTCTGCCAGG
AGAAATATTCAAATATAAATGGACAGTGACTGTAGAAGATGGGCCAACTAAATCAGATCCTCGGTGCCTGACCCGCTATT
ACTCTAGTTTCGTTAATATGGAGAGAGATCTAGCTTCAGGACTCATTGGCCCTCTCCTCATCTGCTACAAAGAATCTGTA
GATCAAAGAGGAAACCAGATAATGTCAGACAAGAGGAATGTCATCCTGTTTTCTGTATTTGATGAGAACCGAAGCTGGTA
CCTCACAGAGAATATACAACGCTTTCTCCCCAATCCAGCTGGAGTGCAGCTTGAGGATCCAGAGTTCCAAGCCTCCAACA
TCATGCACAGCATCAATGGCTATGTTTTTGATAGTTTGCAGTTGTCAGTTTGTTTGCATGAGGTGGCATACTGGTACATT
CTAAGCATTGGAGCACAGACTGACTTCCTTTCTGTCTTCTTCTCTGGATATACCTTCAAACACAAAATGGTCTATGAAGA

FIG. 5A

CACACTCACCCTATTCCCATTCTCAGGAGAAACTGTCTTCATGTCGATGGAAAACCCAGGTCTATGGATTCTGGGGTGCC
ACAACTCAGACTTTCGGAACAGAGGCATGACCGCCTTACTGAAGGTTTCTAGTTGTGACAAGAACACTGGTGATTATTAC
GAGGACAGTTATGAAGATATTTCAGCATACTTGCTGAGTAAAAACAATGCCATTGAACCAAGAAGCTTCGAAATAACTCG
TACTACTCTTCAGTCAGATCAAGAGGAAATTGACTATGATGATACCATATCAGTTGAAATGAAGAAGGAAGATTTTGACA
TTTATGATGAGGATGAAAATCAGAGCCCCCGCAGCTTTCAAAAGAAAACACGACACTATTTTATTGCTGCAGTGGAGAGG
CTCTGGGATTATGGGATGAGTAGCTCCCCACATGTTCTAAGAAACAGGGCTCAGAGTGGCAGTGTCCCTCAGTTCAAGAA
AGTTGTTTTCCAGGAATTTACTGATGGCTCCTTTACTCAGCCCTTATACCGTGGAGAACTAAATGAACATTTGGGACTCC
TGGGGCCATATATAAGAGCAGAAGTTGAAGATAATATCATGGTAACTTTCAGAAATCAGGCCTCTCGTCCCTATTCCTTC
TATTCTAGCCTTATTTCTTATGAGGAAGATCAGAGGCAAGGAGCAGAACCTAGAAAAAACTTTGTCAAGCCTAATGAAAC
CAAAACTTACTTTTGGAAAGTGCAACATCATATGGCACCCACTAAAGATGAGTTTGACTGCAAAGCCTGGGCTTATTTCT
CTGATGTTGACCTGGAAAAAGATGTGCACTCAGGCCTGATTGGACCCCTTCTGGTCTGCCACACTAACACACTGAACCCT
GCTCATGGGAGACAAGTGACAGTACAGGAATTTGCTCTGTTTTTCACCATCTTTGATGAGACCAAAAGCTGGTACTTCAC
TGAAAATATGGAAAGAAACTGCAGGGCTCCCTGCAATATCCAGATGGAAGATCCCACTTTTAAAGAGAATTATCGCTTCC
ATGCAATCAATGGCTACATAATGGATACACTACCTGGCTTAGTAATGGCTCAGGATCAAAGGATTCGATGGTATCTGCTC
AGCATGGGCAGCAATGAAAACATCCATTCTATTCATTTCAGTGGACATGTGTTCACTGTACGAAAAAAAGAGGAGTATAA
AATGGCACTGTACAATCTCTATCCAGGTGTTTTTGAGACAGTGGAAATGTTACCATCCAAAGCTGGAATTTGGCGGGTGG
AATGCCTTATTGGCGAGCATCTACATGCTGGGATGAGCACACTTTTTCTGGTGTACAGCAATAAGTGTCAGACTCCCCTG
GGAATGGCTTCTGGACACATTAGAGATTTTCAGATTACAGCTTCAGGACAATATGGACAGTGGGCCCCAAAGCTGGCCAG
ACTTCATTATTCCGGATCAATCAATGCCTGGAGCACCAAGGAGCCCTTTTCTTGGATCAAGGTGGATCTGTTGGCACCAA
TGATTATTCACGGCATCAAGACCCAGGGTGCCCGTCAGAAGTTCTCCAGCCTCTACATCTCTCAGTTTATCATCATGTAT
AGTCTTGATGGGAAGAAGTGGCAGACTTATCGAGGAAATTCCACTGGAACCTTAATGGTCTTCTTTGGCAATGTGGATTC
ATCTGGGATAAAACACAATATTTTTAACCCTCCAATTATTGCTCGATACATCCGTTTGCACCCAACTCATTATAGCATTC
GCAGCACTCTTCGCATGGAGTTGATGGGCTGTGATTTAAATAGTTGCAGCATGCCATTGGGAATGGAGAGTAAAGCAATA
TCAGATGCACAGATTACTGCTTCATCCTACTTTACCAATATGTTTGCCACCTGGTCTCCTTCAAAAGCTCGACTTCACCT
CCAAGGGAGGAGTAATGCCTGGAGACCTCAGGTGAATAATCCAAAAGAGTGGCTGCAAGTGGACTTCCAGAAGACAATGA
AAGTCACAGGAGTAACTACTCAGGGAGTAAAATCTCTGCTTACCAGCATGTATGTGAAGGAGTTCCTCATCTCCAGCAGT
CAAGATGGCCATCAGTGGACTCTCTTTTTTCAGAATGGCAAAGTAAAGGTTTTTCAGGGAAATCAAGACTCCTTCACACC
TGTGGTGAACTCTCTAGACCCACCGTTACTGACTCGCTACCTTCGAATTCACCCCCAGAGTTGGGTGCACCAGATTGCCC
TGAGGATGGAGGTTCTGGGCTGCGAGGCACAGGACCTCTACTGACTCGAGAATAAAAGATCAGAGCTCTAGAGATCTGTG
TGTTGGTTTTTTGTGTGCGGCCGCAGGAACCCCTAGTGATGGAGTTGGCCACTCCCTCTCTGCGCGCTCGCTCGCTCACT
GAGGCCGGGCGACCAAAGGTCGCCCGACGCCCGGGCTTTGCCCGGGCGGCCTCAGTGAGCGAGCGAGCGCGCAGCTGCCT
GCAGGACATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCC
GCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCG
TTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTC
GGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTG
TGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGAC
TTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTG
GTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAG
TTGGTAGCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGA
AAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACGGGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGAT

FIG. 5B

TTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAAAAATGAAGTTTTAAATCAATCTAAAGTA
TATATGAGTAAACTTGGTCTGACAGTTACCAATGCTTAATCAGTGAGGCACCTATCTCAGCGATCTGTCTATTTCGTTCA
TCCATAGTTGCCTGACTCCCCGTCGTGTAGATAACTACGATACGGGAGGGCTTACCATCTGGCCCCAGTGCTGCAATGAT
ACCGCGAGACCCACGCTCACCGGCTCCAGATTTATCAGCAATAAACCAGCCAGCCGGAAGGGCCGAGCGCAGAAGTGGTC
CTGCAACTTTATCCGCCTCCATCCAGTCTATTAATTGTTGCCGGGAAGCTAGAGTAAGTAGTTCGCCAGTTAATAGTTTG
CGCAACGTTGTTGCCATTGCTACAGGCATCGTGGTGTCACGCTCGTCGTTTGGTATGGCTTCATTCAGCTCCGGTTCCCA
ACGATCAAGGCGAGTTACATGATCCCCCATGTTGTGCAAAAAAGCGGTTAGCTCCTTCGGTCCTCCGATCGTTGTCAGAA
GTAAGTTGGCCGCAGTGTTATCACTCATGGTTATGGCAGCACTGCATAATTCTCTTACTGTCATGCCATCCGTAAGATGC
TTTTCTGTGACTGGTGAGTACTCAACCAAGTCATTCTGAGAATAGTGTATGCGGCGACCGAGTTGCTCTTGCCCGGCGTC
AATACGGGATAATACCGCGCCACATAGCAGAACTTTAAAAGTGCTCATCATTGGAAAACGTTCTTCGGGGCGAAAACTCT
CAAGGATCTTACCGCTGTTGAGATCCAGTTCGATGTAACCCACTCGTGCACCCAACTGATCTTCAGCATCTTTTACTTTC
ACCAGCGTTTCTGGGTGAGCAAAAACAGGAAGGCAAAATGCCGCAAAAAAGGGAATAAGGGCGACACGGAAATGTTGAAT
ACTCATACTCTTCCTTTTTCAATATTATTGAAGCATTTATCAGGGTTATTGTCTCATGAGCGGATACATATTTGAATGTA
TTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTGACGTCTAAGAAACCATTATTATC
ATGACATTAACCTATAAAAATAGGCGTATCACGAGGCCCTTTCGTCTCGCGCGTTTCGGTGATGACGGTGAAAACCTCTG
ACACATGCAGCTCCCGGAGACGGTCACAGCTTGTCTGTAAGCGGATGCCGGGAGCAGACAAGCCCGTCAGGGCGCGTCAG
CGGGTGTTGGCGGGTGTCGGGGCTGGCTTAACTATGCGGCATCAGAGCAGATTGTACTGAGAGTGCACCATAAAATTGTA
AACGTTAATATTTTGTTAAAATTCGCGTTAAATTTTTGTTAAATCAGCTCATTTTTTAACCAATAGGCCGAAATCGGCAA
AATCCCTTATAAATCAAAAGAATAGCCCGAGATAGGGTTGAGTGTTGTTCCAGTTTGGAACAAGAGTCCACTATTAAAGA
ACGTGGACTCCAACGTCAAAGGGCGAAAAACCGTCTATCAGGGCGATGGCCCACTACGTGAACCATCACCCAAATCAAGT
TTTTTGGGGTCGAGGTGCCGTAAAGCACTAAATCGGAACCCTAAAGGGAGCCCCCGATTTAGAGCTTGACGGGGAAAGCC
GGCGAACGTGGCGAGAAAGGAAGGGAAGAAAGCGAAAGGAGCGGGCGCTAGGGCGCTGGCAAGTGTAGCGGTCACGCTGC
GCGTAACCACCACACCCGCCGCGCTTAATGCGCCGCTACAGGGCGCGTACTATGGTTGCTTTGACGTATGCGGTGTGAAA
TACCGCACAGATGCGTAAGGAGAAAATACCGCATCAGGCCGTAACCTGTCGGATCACCGGAAAGGACCCGTAAAGTGATA
ATGATTATCATCTACATATCACAACGTGCGTGGAGGCCATCAAACCACGTCAAATAATCAATTATGACGCAGGTATCGTA
TTAATTGATCTGCATCAACTTAACGTAAAAACAACTTCAGACAATACAAATCAGCGACACTGAATACGGGGCAACCTCAT
GTCAACGAAGAACAGAACCCGCAGAACAACAACCCGCAACATCCGCTTTCCTAACCAAATGATTGAACAAATTAACATCG
CTCTTGAGCAAAAAGGGTCCGGGAATTTCTCAGCCTGGGTCATTGAAGCCTGCCGTCGGAGACTAACGTCAGAAAAGAGA
GCATATACATCAATTAAAAGTGATGAAGAATGAACATCCCGCGTTCTTCCCTCCGAACAGGACGATATTGTAAATTCACT
TAATTACGAGGGCATTGCAGTAATTGAGTTGCAGTTTTACCACTTTCCTGACAGTGACAGACTGCGTGTTGGCTCTGTCA
CAGACTAAATAGTTTGAATGATTAGCAGTTATGGTGATCAGTCAACCACCAGGGAATAATCCTTCATATTATTATCGTGC
TTCACCAACGCTGCCTCAATTGCTCTGAATGCTTCCAGAGACACCTTATGTTCTATACATGCAATTACAACATCAGGGTA
ACTCATAGAAATGGTGCTATTAAGCATATTTTTTACACGAATCAGATCCACGGAGGGATCATCAGCAGATTGTTCTTTAT
TCATTTTGTCGCTCCATGCGCTTGCTCTTCATCTAGCGGTTAAAATATTACTTCAAATCTTTCTGTATGAAGATTTGAGC
ACGTTGGCCTTACATACATCTGTCGGTTGTATTTCCCTCCAGAATGCCAGCAGGACCGCACTTTGTTACGCAACCAATAC
TATTAAGTGAAAACATTCCTAATATTTGACATAAATCATCAACAAAACACAAGGAGGTCAGACCAGATTGAAACGATAAA
AACGATAATGCAAACTACGCGCCCTCGTATCACATGGAAGGTTTTACCAATGGCTCAGGTTGCCATTTTTAAAGAAATAT
TCGATCAAGTGCGAAAAGATTTAGACTGTGAATTGTTTTATTCTGAACTAAAACGTCACAACGTCTCACATTATATTTAC
TATCTAGCCACAGATAATATTCACATCGTGTTAGAAAACGATAACACCGTGTTAATAAAAGGACTTAAAAAGGTTGTAAA
TGTTAAATTCTCAAGAAACACGCATCTTATAGAAACGTCCTATGATAGGTTGAAATCAAGAGAAATCACATTTCAGCAAT
ACAGGGAAAATCTTGCTAAAGCAGGAGTTTTCCGATGGGTTACAAATATCCATGAACATAAAAGATATTACTATACCTTT

FIG. 5C

GATAATTCATTACTATTTACTGAGAGCATTCAGAACACTACACAAATCTTTCCACGCTAAATCATAACGTCCGGTTTCTT
CCGTGTCAGCACCGGGGCGTTGGCATAATGCAATACGTGTACGCGCTAAACCCTGTGTGCATCGTTTTAATTATTCCCGG
ACACTCCCGCAGAGAAGTTCCCCGTCAGGGCTGTGGACATAGTTAATCCGGGAATACAATGACGATTCATCGCACCTGAC
ATACATTAATAAATATTAACAATATGAAATTTCAACTCATTGTTTAGGGTTTGTTTAATTTTCTACACATACGATTCTGC
GAACTTCAAAAAGCATCGGGAATAACACCATGAAAAAAATGCTACTCGCTACTGCGCTGGCCCTGCTTATTACAGGATGT
GCTCAACAGACGTTTACTGTTCAAAACAAACCGGCAGCAGTAGCACCAAAGGAAACCATCACCCATCATTTCTTCGTTTC
TGGAATTGGGCAGAAGAAAACTGTCGATGCAGCCAAAATTTGTGGCGGCGCAGAAAATGTTGTTAAAACAGAAACCCAGC
AAACATTCGTAAATGGATTGCTCGGTTTTATTACTTTAGGCATTTATACTCCGCTGGAAGCGCGTGTGTATTGCTCACAA
TAATTGCATGAGTTGCCCATCGCGATATGGGCAACTCTATCTGCACTGCTCATTAATATACTTCTGGGTTCCTTCCAGTT
GTTTTTGCATAGTGATCAGCCTCTCTCTGAGGGTGAAATAATCCCGTTCAGCGGTGTCTGCCAGTCGGGGGGAGGCTGCA
TTATCCACGCCGGAGGCGGTGGTGGCTTCACGCACTGACTGACAGACTGCTTTGATGTGCAACCGACGACGACCAGCGGC
AACATCATCACGCAGAGCATCATTTTCAGCTTTAGCATCAGCTAACTCCTTCGTGTATTTTGCATCGAGCGCAGCAACAT
CACGCTGACGCATCTGCATGTCAGTAATTGCCGCGTTCGCCAGCTTCAGTTCTCTGGCATTTTTGTCGCGCTGGGCTTTG
TAGGTAATGGCGTTATCACGGTAATGATTAACAGCCCATGACAGGCAGACGATGATGCAGATAACCAGAGCGGAGATAAT
CGCGGTGACTCTGCTCATACATCAATCTCTCTGACCGTTCCGCCCGCTTCTTTGAATTTTGCAATCAGGCTGTCAGCCTT
ATGCTCGAACTGACCATAACCAGCGCCCGGCAGTGAAGCCCAGATATTGCTGCAACGGTCGATTGCCTGACGGATATCAC
CACGATCAATCATAGGTAAAGCGCCACGCTCCTTAATCTGCTGCAATGCCACAGCGTCCTGACTTTTCGGAGAGAAGTCT
TTCAGGCCAAGCTGCTTGCGGTAGGCATCCCACCAACGGGAAAGAAGCTGGTAGCGTCCGGCGCCTGTTGATTTGAGTTT
TGGGTTTAGCGTGACAAGTTTGCGAGGGTGATCGGAGTAATCAGTAAATAGCTCTCCGCCTACAATGACGTCATAACCAT
GATTTCTGGTTTTCTGACGTCCGTTATCAGTTCCCTCCGACCACGCCAGCATATCGAGGAACGCCTTACGTTGATTATTG
ATTTCTACCATCTTCTACTCCGGCTTTTTTAGCAGCGAAGCGTTTGATAAGCGAACCAATCGAGTCAGTACCGATGTAGC
CGATAAACACGCTCGTTATATAAGCGAGATTGCTACTTAGTCCGGCGAAGTCGAGAAGGTCACGAATGAACCAGGCGATA
ATGGCGCACATCGTTGCGTCGATTACTGTTTTTGTAAACGCACCGCCATTATATCTGCCGCGAAGGTACGCCATTGCAAA
CGCAAGGATTGCCCCGATGCCTTGTTCCTTTGCCGCGAGAATGGCGGCCAACAGGTCATGTTTTTCTGGCATCTTCATGT
CTTACCCCCAATAAGGGGATTTGCTCTATTTAATTAGGAATAAGGTCGATTACTGATAGAACAAATCCAGGCTACTGTGT
TTAGTAATCAGATTTGTTCGTGACCGATATGCACGGGCAAAACGGCAGGAGGTTGTTAGCGCGACCTCCTGCCACCCGCT
TTCACGAAGGTCATGTGTAAAAGGCCGCAGCGTAACTATTACTAATGAATTCAGGACAGACAGTGGCTACGGCTCAGTTT
GGGTTGTGCTGTTGCTGGGCGGCGATGACGCCTGTACGCATTTGGTGATCCGGTTCTGCTTCCGGTATTCGCTTAATTCA
GCACAACGGAAAGAGCACTGGCTAACCAGGCTCGCCGACTCTTCACGATTATCGACTCAATGCTCTTACCTGTTGTGCAG
ATATAAAAAATCCCGAAACCGTTATGCAGGCTCTAACTATTACCTGCGAACTGTTTCGGGATTGCATTTTGCAGACCTCT
CTGCCTGCGATGGTTGGAGTTCCAGACGATACGTCGAAGTGACCAACTAGGCGGAATCGGTAGTAAGCGCCGCCTCTTTT
CATCTCACTACCACAACGAGCGAATTAACCCATCGTTGAGTCAAATTTACCCAATTTTATTCAATAAGTCAATATCATGC
CGTTAATATGTTGCCATCCGTGGCAATCATGCTGCTAACGTGTGACCGCATTCAAAATGTTGTCTGCGATTGACTCTTCT
TTGTGGCATTGCACCACCAGAGCGTCATACAGCGGCTTAACAGTGCGTGACCAGGTGGGTTGGGTAAGGTTTGGGATTAG
CATCGTCACAGCGCGATATGCTGCGCTTGCTGGCATCCTTGAATAGCCGACGCCTTTGCATCTTCCGCACTCTTTCTCGA
CAACTCTCCCCCACAGCTCTGTTTTGGCAATATCAACCGCACGGCCTGTACCATGGCAATCTCTGCATCTTGCCCCCGGC
GTCGCGGCACTACGGCAATAATCCGCATAAGCGAATGTTGCGAGCACTTGCAGTACCTTTGCCTTAGTATTTCCTTCAAG
CTGCCCCTGCAGG

FIG. 5D

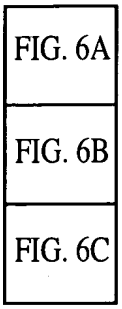

FIG. 6

CGCCCCTGCAGGCAGCTGCGCGCTCGCTCGCTCACTGAGGCCGCCCGGGCAA
AGCCCGGGCGTCGGGCGACCTTTGGTCGCCCGGCCTCAGTGAGCGAGCGAGC
GCGCAGAGAGGGAGTGGCCAACTCCATCACTAGGGGTTCCTGCGGCCGCACG
CGTGGTGGCGCGGGGTAAACTGGGAAAGTGATGTCGTGTACTGGCTCCGCCT
TTTTCCCGAGGGTGGGGGAGAACCGTATATAAGTGCAGTAGTCGCCGTGAAC
GTTCTTTTTCGCAACGGGTTTGCCGCCCCGCGGCAGGTAAGTGCCAGGGAAT
GTTTGTTCTTAAATACCATCGCTCCAGGGAATGTTTGTTCTTAAATACCATC
TACTGACACTGACATCCACTTTTTCTTTTTCTCCACAGGTATCGATCCACCA
TGCAAATAGAGCTCTCCACCTGCTTCTTTCTGTGCCTTTTGCGATTCTGCTT
TAGTGCCACCAGAAGATACTACCTGGGTGCAGTGGAACTGTCATGGGACTAT
ATGCAAAGTGATCTCGGTGAGCTGCCTGTGGACGCAAGATTTCCTCCTAGAG
TGCCAAAATCTTTTCCATTCAACACCTCAGTCGTGTACAAAAAGACTCTGTT
TGTAGAATTCACGGATCACCTTTTCAACATCGCTAAGCCAAGGCCACCCTGG
ATGGGTCTGCTAGGTCCTACCATCCAGGCTGAGGTTTATGATACAGTGGTCA
TTACACTTAAGAACATGGCTTCCCATCCTGTCAGTCTTCATGCTGTTGGTGT
ATCCTACTGGAAAGCTTCTGAGGGAGCTGAATATGATGATCAGACCAGTCAA
AGGGAGAAAGAAGATGATAAAGTCTTCCCTGGTGGAAGCCATACATATGTCT
GGCAGGTCCTGAAAGAGAATGGTCCAATGGCCTCTGACCCACTGTGCCTTAC
CTACTCATATCTTTCTCATGTGGACCTGGTAAAAGACTTGAATTCAGGCCTC
ATTGGAGCCCTACTAGTATGTAGAGAAGGGAGTCTGGCCAAGGAAAAGACAC
AGACCTTGCACAAATTTATACTACTTTTTGCTGTATTTGATGAAGGGAAAAG
TTGGCACTCAGAAACAAAGAACTCCTTGATGCAGGATAGGGATGCTGCATCT
GCTCGGGCCTGGCCTAAAATGCACACAGTCAATGGTTATGTAAACAGGTCTC
TGCCAGGTCTGATTGGATGCCACAGGAAATCAGTCTATTGGCATGTGATTGG
AATGGGCACCACTCCTGAAGTGCACTCAATATTCCTCGAAGGTCACACATTT
CTTGTGAGGAACCATCGCCAGGCGTCCTTGGAAATCTCGCCAATAACTTTCC
TTACTGCTCAAACACTCTTGATGGACCTTGGACAGTTTCTACTGTTTTGTCA
TATCTCTTCCCACCAACATGATGGCATGGAAGCTTATGTCAAAGTAGACAGC
TGTCCAGAGGAACCCCAACTACGAATGAAAAATAATGAAGAAGCGGAAGACT
ATGATGATGATCTTACTGATTCTGAAATGGATGTGGTCAGGTTTGATGATGA
CAACTCTCCTTCCTTTATCCAAATTCGCTCAGTTGCCAAGAAGCATCCTAAA

FIG. 6A

ACTTGGGTACATTACATTGCTGCTGAAGAGGAGGACTGGGACTATGCTCCCT
TAGTCCTCGCCCCCGATGACAGAAGTTATAAAAGTCAATATTTGAACAATGG
CCCTCAGCGGATTGGTAGGAAGTACAAAAAAGTCCGATTTATGGCATACACA
GATGAAACCTTTAAGACTCGTGAAGCTATTCAGCATGAATCAGGAATCTTGG
GACCTTTACTTTATGGGGAAGTTGGAGACACACTGTTGATTATATTTAAGAA
TCAAGCAAGCAGACCATATAACATCTACCCTCACGGAATCACTGATGTCCGT
CCTTTGTATTCAAGGAGATTACCAAAAGGTGTAAAACATTTGAAGGATTTTC
CAATTCTGCCAGGAGAAATATTCAAATATAAATGGACAGTGACTGTAGAAGA
TGGGCCAACTAAATCAGATCCTCGGTGCCTGACCCGCTATTACTCTAGTTTC
GTTAATATGGAGAGAGATCTAGCTTCAGGACTCATTGGCCCTCTCCTCATCT
GCTACAAAGAATCTGTAGATCAAAGAGGAAACCAGATAATGTCAGACAAGAG
GAATGTCATCCTGTTTTCTGTATTTGATGAGAACCGAAGCTGGTACCTCACA
GAGAATATACAACGCTTTCTCCCCAATCCAGCTGGAGTGCAGCTTGAGGATC
CAGAGTTCCAAGCCTCCAACATCATGCACAGCATCAATGGCTATGTTTTTGA
TAGTTTGCAGTTGTCAGTTTGTTTGCATGAGGTGGCATACTGGTACATTCTA
AGCATTGGAGCACAGACTGACTTCCTTTCTGTCTTCTTCTCTGGATATACCT
TCAAACACAAAATGGTCTATGAAGACACACTCACCCTATTCCCATTCTCAGG
AGAAACTGTCTTCATGTCGATGGAAAACCCAGGTCTATGGATTCTGGGGTGC
CACAACTCAGACTTTCGGAACAGAGGCATGACCGCCTTACTGAAGGTTTCTA
GTTGTGACAAGAACACTGGTGATTATTACGAGGACAGTTATGAAGATATTTC
AGCATACTTGCTGAGTAAAAACAATGCCATTGAACCAAGAAGCTTCTCCCAG
AATCCACCAGTCTTGAAACGCCATCAACGCGAAATAACTCGTACTACTCTTC
AGTCAGATCAAGAGGAAATTGACTATGATGATACCATATCAGTTGAAATGAA
GAAGGAAGATTTTGACATTTATGATGAGGATGAAAATCAGAGCCCCCGCAGC
TTTCAAAAGAAAACACGACACTATTTTATTGCTGCAGTGGAGAGGCTCTGGG
ATTATGGGATGAGTAGCTCCCCACATGTTCTAAGAAACAGGGCTCAGAGTGG
CAGTGTCCCTCAGTTCAAGAAAGTTGTTTTCCAGGAATTTACTGATGGCTCC
TTTACTCAGCCCTTATACCGTGGAGAACTAAATGAACATTTGGGACTCCTGG
GGCCATATATAAGAGCAGAAGTTGAAGATAATATCATGGTAACTTTCAGAAA
TCAGGCCTCTCGTCCCTATTCCTTCTATTCTAGCCTTATTTCTTATGAGGAA
GATCAGAGGCAAGGAGCAGAACCTAGAAAAAACTTTGTCAAGCCTAATGAAA
CCAAAACTTACTTTTGGAAAGTGCAACATCATATGGCACCCACTAAAGATGA
GTTTGACTGCAAAGCCTGGGCTTATTTCTCTGATGTTGACCTGGAAAAAGAT
GTGCACTCAGGCCTGATTGGACCCCTTCTGGTCTGCCACACTAACACACTGA
ACCCTGCTCATGGGAGACAAGTGACAGTACAGGAATTTGCTCTGTTTTTCAC
CATCTTTGATGAGACCAAAAGCTGGTACTTCACTGAAAATATGGAAAGAAAC
TGCAGGGCTCCCTGCAATATCCAGATGGAAGATCCCACTTTTAAAGAGAATT
ATCGCTTCCATGCAATCAATGGCTACATAATGGATACACTACCTGGCTTAGT
AATGGCTCAGGATCAAAGGATTCGATGGTATCTGCTCAGCATGGGCAGCAAT

FIG. 6B

GAAAACATCCATTCTATTCATTTCAGTGGACATGTGTTCACTGTACGAAAAA
AAGAGGAGTATAAAATGGCACTGTACAATCTCTATCCAGGTGTTTTTGAGAC
AGTGGAAATGTTACCATCCAAAGCTGGAATTTGGCGGGTGGAATGCCTTATT
GGCGAGCATCTACATGCTGGGATGAGCACACTTTTTCTGGTGTACAGCAATA
AGTGTCAGACTCCCCTGGGAATGGCTTCTGGACACATTAGAGATTTTCAGAT
TACAGCTTCAGGACAATATGGACAGTGGGCCCCAAAGCTGGCCAGACTTCAT
TATTCCGGATCAATCAATGCCTGGAGCACCAAGGAGCCCTTTTCTTGGATCA
AGGTGGATCTGTTGGCACCAATGATTATTCACGGCATCAAGACCCAGGGTGC
CCGTCAGAAGTTCTCCAGCCTCTACATCTCTCAGTTTATCATCATGTATAGT
CTTGATGGGAAGAAGTGGCAGACTTATCGAGGAAATTCCACTGGAACCTTAA
TGGTCTTCTTTGGCAATGTGGATTCATCTGGGATAAAACACAATATTTTTAA
CCCTCCAATTATTGCTCGATACATCCGTTTGCACCCAACTCATTATAGCATT
CGCAGCACTCTTCGCATGGAGTTGATGGGCTGTGATTTAAATAGTTGCAGCA
TGCCATTGGGAATGGAGAGTAAAGCAATATCAGATGCACAGATTACTGCTTC
ATCCTACTTTACCAATATGTTTGCCACCTGGTCTCCTTCAAAAGCTCGACTT
CACCTCCAAGGGAGGAGTAATGCCTGGAGACCTCAGGTGAATAATCCAAAAG
AGTGGCTGCAAGTGGACTTCCAGAAGACAATGAAAGTCACAGGAGTAACTAC
TCAGGGAGTAAAATCTCTGCTTACCAGCATGTATGTGAAGGAGTTCCTCATC
TCCAGCAGTCAAGATGGCCATCAGTGGACTCTCTTTTTTCAGAATGGCAAAG
TAAAGGTTTTTCAGGGAAATCAAGACTCCTTCACACCTGTGGTGAACTCTCT
AGACCCACCGTTACTGACTCGCTACCTTCGAATTCACCCCCAGAGTTGGGTG
CACCAGATTGCCCTGAGGATGGAGGTTCTGGGCTGCGAGGCACAGGACCTCT
ACTGACTCGAGCCTAATAAAGGAAATTTATTTTCATTGCAATAGTGTGTTGG
TTTTTTGTGTGCGGCCGCAGGAACCCCTAGTGATGGAGTTGGCCACTCCCTC
TCTGCGCGCTCGCTCGCTCACTGAGGCCGGGCGACCAAAGGTCGCCCGACGC
CCGGGCTTTGCCCGGGCGGCCTCAGTGAGCGAGCGAGCGCGCAGCTGCCTGC
AGGACAT

FIG. 6C

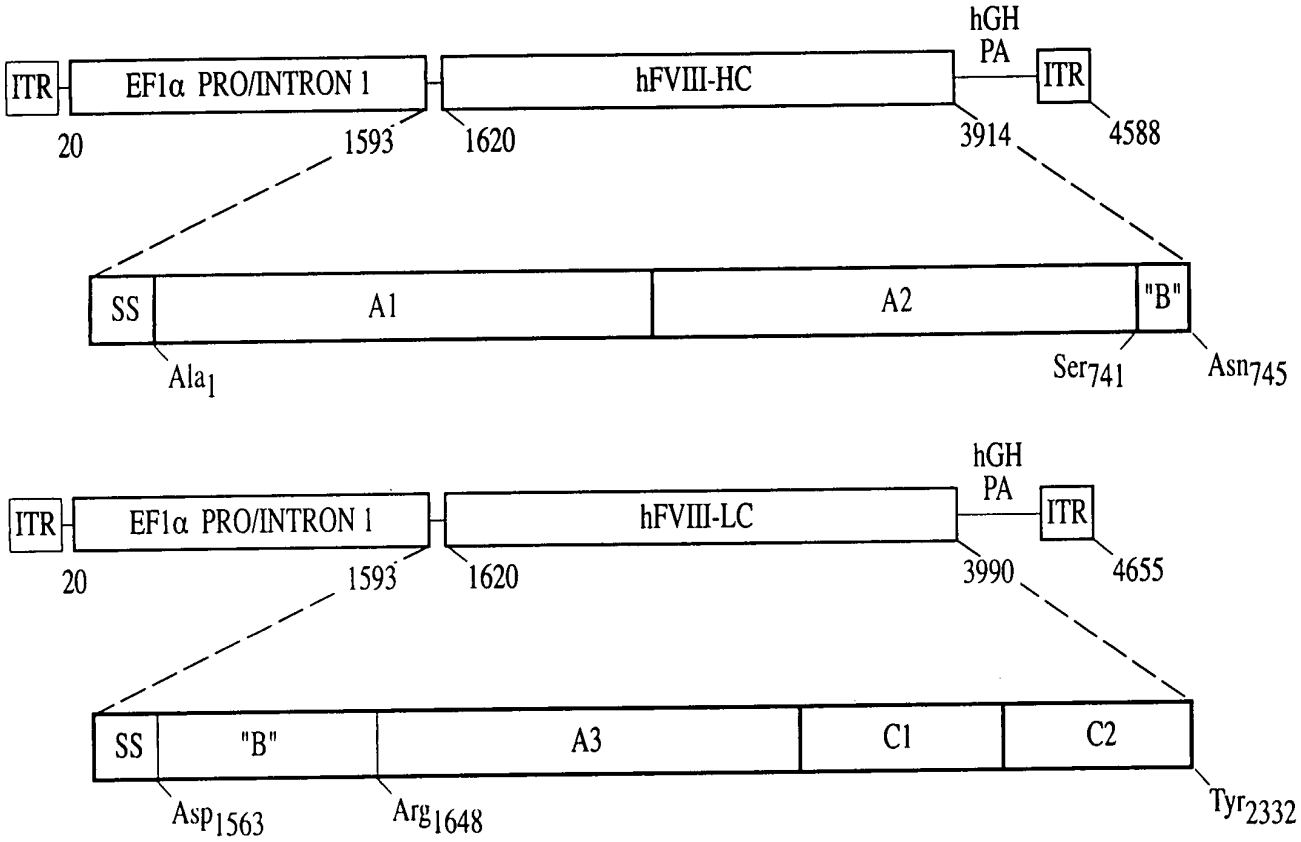
ITR
EF1α PRO/INTRON 1
hFVIII-HC
hGH PA
ITR
20
1593
1620
3914
4588
SS
A1
A2
"B"
Ala1
Ser741
Asn745
ITR
EF1α PRO/INTRON 1
hFVIII-LC
hGH PA
ITR
20
1593
1620
3990
4655
SS
"B"
A3
C1
C2
Asp1563
Arg1648
Tyr2332

FIG. 7

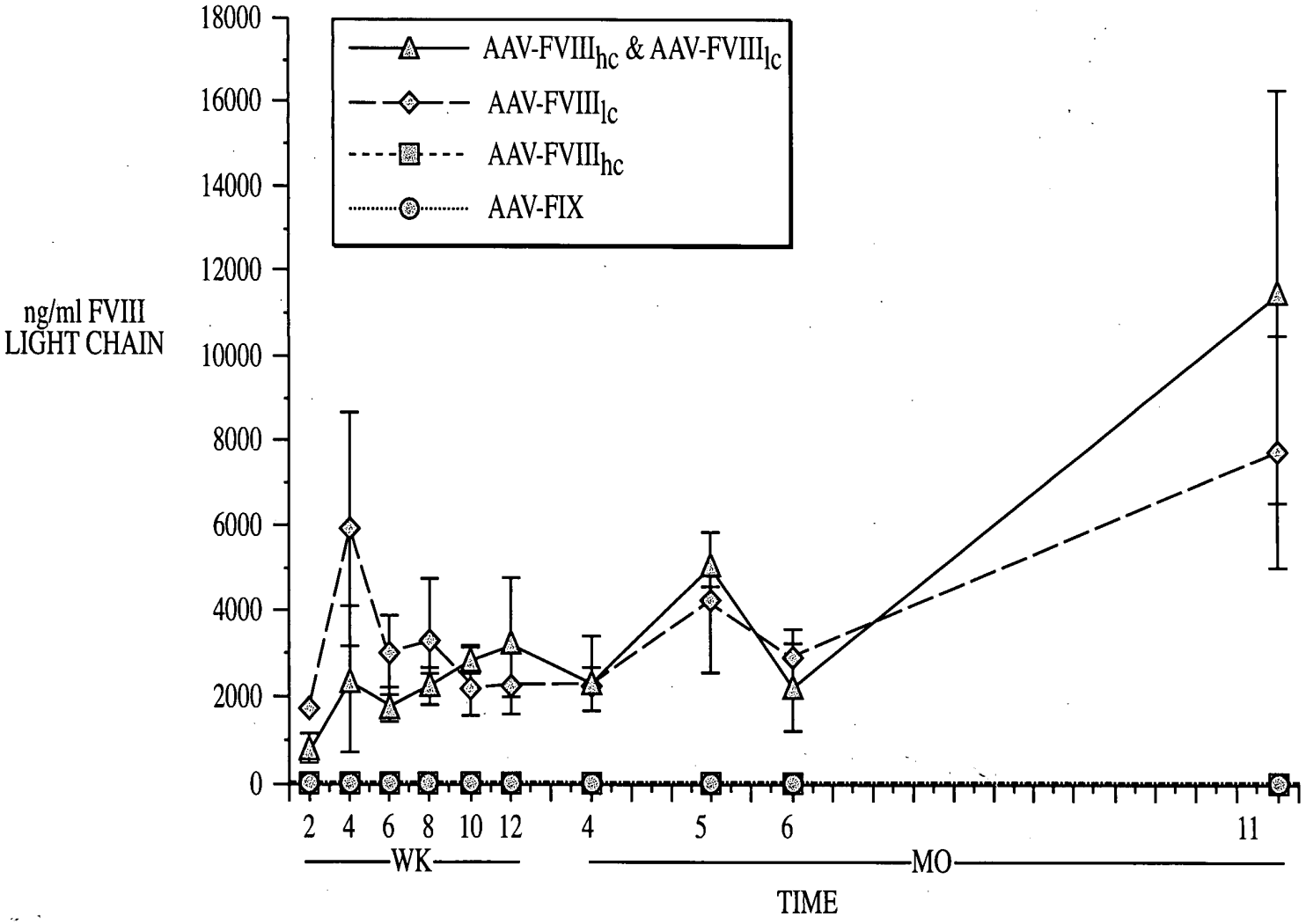
AAV-FVIII$_{hc}$ & AAV-FVIII$_{lc}$
AAV-FVIII$_{lc}$
AAV-FVIII$_{hc}$
AAV-FIX
ng/ml FVIII
LIGHT CHAIN
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
2 4 6 8 10 12 4 5 6 11
WK
MO
TIME

FIG. 8

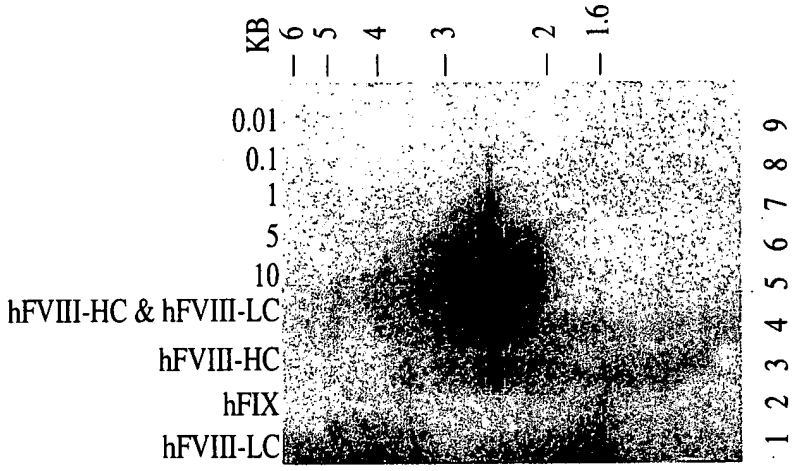
KB
6
5
4
3
2
1.6
0.01
0.1
1
5
10
hFVIII-HC & hFVIII-LC
hFVIII-HC
hFIX
hFVIII-LC
1 2 3 4 5 6 7 8 9

FIG. 9B

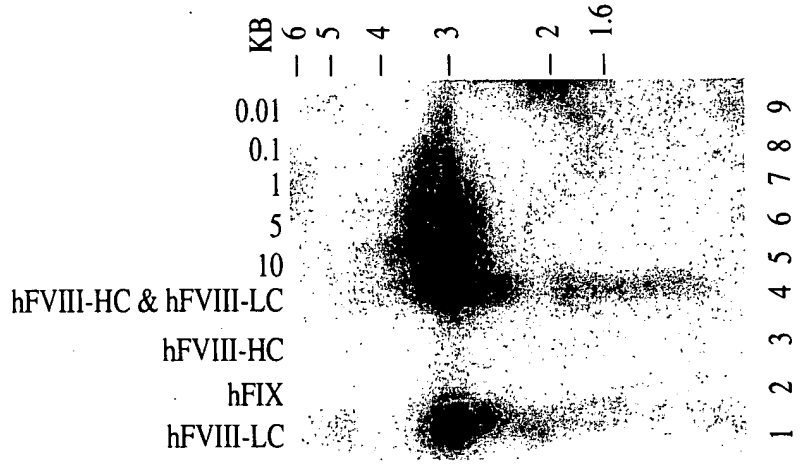
KB
6
5
4
3
2
1.6
0.01
0.1
1
5
10
hFVIII-HC & hFVIII-LC
hFVIII-HC
hFIX
hFVIII-LC
1 2 3 4 5 6 7 8 9

FIG. 9A

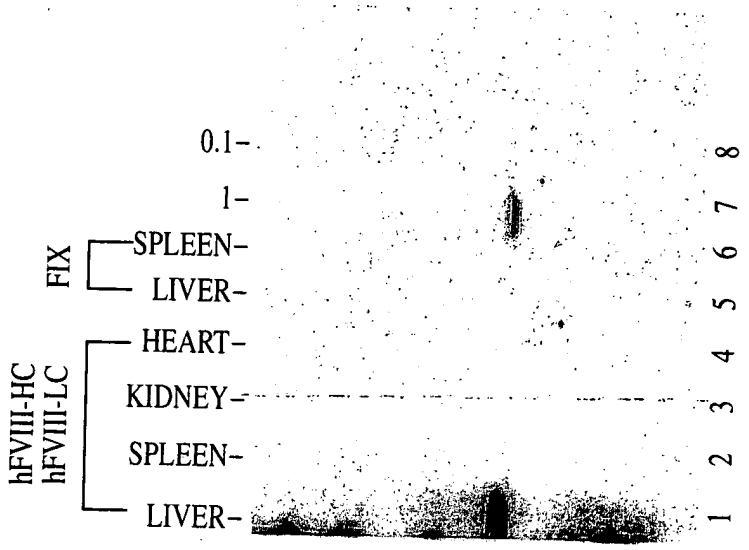

FIG. 10B

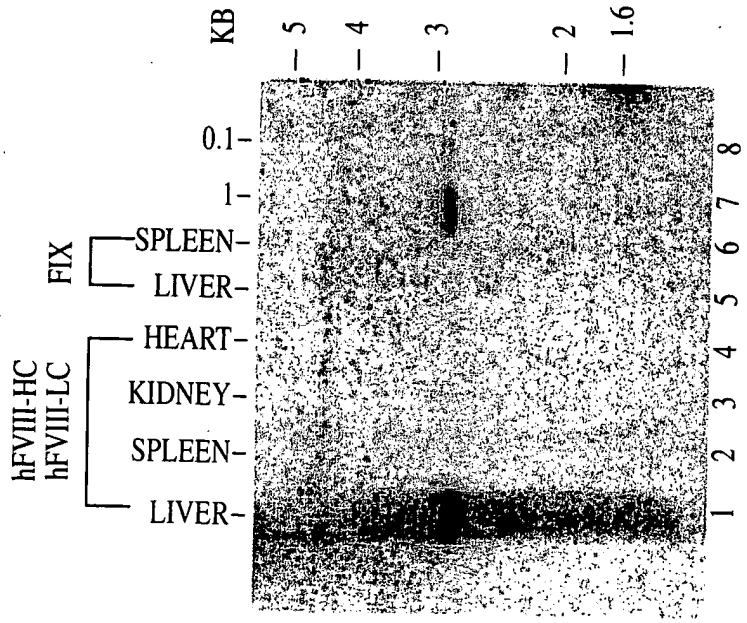

FIG. 10A

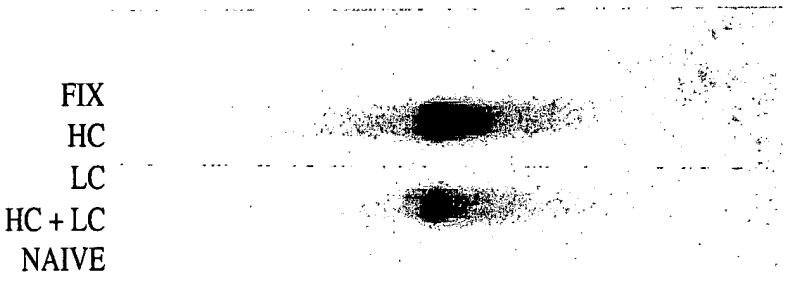

FIG. 11B

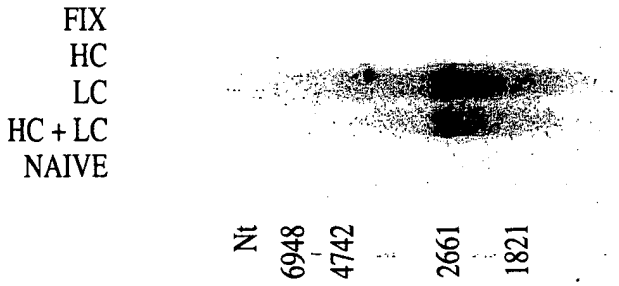

FIG. 11A